304D Pg 1/10

CRF Errors Corrected by the STIC System Branch

Serial Number: 10/037,044

CRF Processing Date: 2/14/2002

Edited by:

Verified by: _____ (STIC staff)

ENTERED

- ☐ Changed a file from non-ASCII to ASCII
- ☐ Changed the margins in cases where the sequence text was "wrapped" down to the next line.
- ☐ Edited a format error in the Current Application Data section, specifically: #6/Raw
- ☐ Edited the Current Application Data section with the actual current number. The number inputted by the applicant was ☐ the prior application data; or ☐ other _____. 5 6
- ☐ Added the mandatory heading and subheadings for "Current Application Data".
- ☐ Edited the "Number of Sequences" field. The applicant spelled out a number instead of using an integer.
- ☐ Changed the spelling of a mandatory field (the headings or subheadings), specifically:
- ☐ Corrected the SEQ ID NO when obviously incorrect. The sequence numbers that were edited were:
- ☐ Inserted or corrected a nucleic number at the end of a nucleic line. SEQ ID NO's edited:
- ☐ Corrected subheading placement. All responses must be on the same line as each subheading. If the applicant placed a response below the subheading, this was moved to its appropriate place.
- ☐ Inserted colons after headings/subheadings. Headings edited included:
- ☐ Deleted extra, invalid, headings used by an applicant, specifically:
- ☑ Deleted: ☑ non-ASCII "garbage" at the beginning/end of files; ☐ secretary initials/filename at end of file; ☐ page numbers throughout text; ☐ other invalid text, such as _____.
- ☐ Inserted mandatory headings, specifically: _____
- ☐ Corrected an obvious error in the response, specifically:
- ☐ Edited identifiers where upper case is used but lower case is required, or vice versa.
- ☐ Corrected an error in the Number of Sequences field, specifically:
- ☐ A "Hard Page Break" code was inserted by the applicant. All occurrences had to be deleted.
- ☐ Deleted *ending* stop codon in amino acid sequences and adjusted the "(A)Length:" field accordingly (error due to a PatentIn bug). Sequences corrected: _____
- ☐ Other:

*Examiner: The above corrections must be communicated to the applicant in the first Office Action. DO NOT send a copy of this form.

3/1/95

10/Raw Seq

PCT10

RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/031,044

DATE: 02/14/2002
TIME: 09:03:29

Input Set : A:\PTO.AMC.txt
Output Set: N:\CRF3\02142002\J031044.raw

```
      3 <110> APPLICANT: C. Frank Bennett
      4       Lex M. Cowsert
      5       ISIS PHARMACEUTICALS, INC.
      7 <120> TITLE OF INVENTION: ANTISENSE MODULATION OF SHP-2 EXPRESSION
      9 <130> FILE REFERENCE: RTSP-0252
C--> 11 <140> CURRENT APPLICATION NUMBER: US/10/031,044
C--> 11 <141> CURRENT FILING DATE: 2002-01-14
     11 <150> PRIOR APPLICATION NUMBER: 09/358,683
     12 <151> PRIOR FILING DATE: 1999-07-21
     14 <160> NUMBER OF SEQ ID NOS: 47
     16 <210> SEQ ID NO: 1
     17 <211> LENGTH: 2121
     18 <212> TYPE: DNA
     19 <213> ORGANISM: Homo sapiens
     21 <220> FEATURE:
     22 <221> NAME/KEY: CDS
     23 <222> LOCATION: (154)..(1935)
     25 <400> SEQUENCE: 1
     26 cgccaggcct ggaggggggt ctgtgcgcgg ccggctggct ctgccccgcg tccggtcccg   60
     28 agcgggcctc cctcgggcca gcccgatgtg accgagccca gcggagcctg agcaaggagc  120
     30 gggtccgtcg cggagccgga gggcgggagg aac atg aca tcg cgg aga tgg        171
     31                                     Met Thr Ser Arg Arg Trp
     32                                       1               5
     34 ttt cac cca aat atc act ggt gtg gag gca gaa aac cta ctg ttg aca     219
     35 Phe His Pro Asn Ile Thr Gly Val Glu Ala Glu Asn Leu Leu Leu Thr
     36              10                  15                  20
     38 aga gga gtt gat ggc agt ttt ttg gca agg cct agt aaa agt aac cct     267
     39 Arg Gly Val Asp Gly Ser Phe Leu Ala Arg Pro Ser Lys Ser Asn Pro
     40          25                  30                  35
     42 gga gac ttc aca ctt tcc gtt aga aga aat gga gct gtc acc cac atc     315
     43 Gly Asp Phe Thr Leu Ser Val Arg Arg Asn Gly Ala Val Thr His Ile
     44      40                  45                  50
     46 aag att cag aac act ggt gat tac tat gac ctg tat gga ggg gag aaa     363
     47 Lys Ile Gln Asn Thr Gly Asp Tyr Tyr Asp Leu Tyr Gly Gly Glu Lys
     48  55                  60                  65                  70
     50 ttt gcc act ttg gct gag ttg gtc cag tat tac atg gaa cat cac ggg     411
     51 Phe Ala Thr Leu Ala Glu Leu Val Gln Tyr Tyr Met Glu His His Gly
     52                  75                  80                  85
     54 caa tta aaa gag aag aat gga gat gtc att gag ctt aaa tat cct ctg     459
     55 Gln Leu Lys Glu Lys Asn Gly Asp Val Ile Glu Leu Lys Tyr Pro Leu
     56              90                  95                  100
     58 aac tgt gca gat cct acc tct gaa agg tgg ttt cat gga cat ctc tct     507
     59 Asn Cys Ala Asp Pro Thr Ser Glu Arg Trp Phe His Gly His Leu Ser
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RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/031,044

DATE: 02/14/2002
TIME: 09:03:29

Input Set : A:\PTO.AMC.txt
Output Set: N:\CRF3\02142002\J031044.raw

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62 ggg aaa gaa gca gag aaa tta tta act gaa aaa gga aaa cat ggt agt      555
63 Gly Lys Glu Ala Glu Lys Leu Leu Thr Glu Lys Gly Lys His Gly Ser
64      120                 125                 130
66 ttt ctt gta cga gag agc cag agc cac cct gga gat ttt gtt ctt tct      603
67 Phe Leu Val Arg Glu Ser Gln Ser His Pro Gly Asp Phe Val Leu Ser
68 135                 140                 145                 150
70 gtg cgc act ggt gat gac aaa ggg gag agc aat gac ggc aag tct aaa      651
71 Val Arg Thr Gly Asp Asp Lys Gly Glu Ser Asn Asp Gly Lys Ser Lys
72                  155                 160                 165
74 gtg acc cat gtt atg att cgc tgt cag gaa ctg aaa tac gac gtt ggt      699
75 Val Thr His Val Met Ile Arg Cys Gln Glu Leu Lys Tyr Asp Val Gly
76              170                 175                 180
78 gga gga gaa cgg ttt gat tct ttg aca gat ctt gtg gaa cat tat aag      747
79 Gly Gly Glu Arg Phe Asp Ser Leu Thr Asp Leu Val Glu His Tyr Lys
80          185                 190                 195
82 aag aat cct atg gtg gaa aca ttg ggt aca gta cta caa ctc aag cag      795
83 Lys Asn Pro Met Val Glu Thr Leu Gly Thr Val Leu Gln Leu Lys Gln
84      200                 205                 210
86 ccc ctt aac acg act cgt ata aat gct gct gaa ata gaa agc aga gtt      843
87 Pro Leu Asn Thr Thr Arg Ile Asn Ala Ala Glu Ile Glu Ser Arg Val
88 215                 220                 225                 230
90 cga gaa cta agc aaa tta gct gag acc aca gat aaa gtc aaa caa ggc      891
91 Arg Glu Leu Ser Lys Leu Ala Glu Thr Thr Asp Lys Val Lys Gln Gly
92                  235                 240                 245
94 ttt tgg gaa gaa ttt gag aca cta caa caa cag gag tgc aaa ctt ctc      939
95 Phe Trp Glu Glu Phe Glu Thr Leu Gln Gln Gln Glu Cys Lys Leu Leu
96              250                 255                 260
98 tac agc cga aaa gag ggt caa agg caa gaa aac aaa aac aaa aat aga      987
99 Tyr Ser Arg Lys Glu Gly Gln Arg Gln Glu Asn Lys Asn Lys Asn Arg
100         265                 270                 275
102 tat aaa aac atc ctg ccc ttt gat cat acc agg gtt gtc cta cac gat    1035
103 Tyr Lys Asn Ile Leu Pro Phe Asp His Thr Arg Val Val Leu His Asp
104     280                 285                 290
106 ggt gat ccc aat gag cct gtt tca gat tac atc aat gca aat atc atc    1083
107 Gly Asp Pro Asn Glu Pro Val Ser Asp Tyr Ile Asn Ala Asn Ile Ile
108 295                 300                 305                 310
110 atg cct gaa ttt gaa acc aag tgc aac aat tca aag ccc aaa aag agt    1131
111 Met Pro Glu Phe Glu Thr Lys Cys Asn Asn Ser Lys Pro Lys Lys Ser
112                 315                 320                 325
114 tac att gcc aca caa ggc tgc ctg caa aac acg gtg aat gac ttt tgg    1179
115 Tyr Ile Ala Thr Gln Gly Cys Leu Gln Asn Thr Val Asn Asp Phe Trp
116             330                 335                 340
118 cgg atg gtg ttc caa gaa aac tcc cga gtg att gtc atg aca acg aaa    1227
119 Arg Met Val Phe Gln Glu Asn Ser Arg Val Ile Val Met Thr Thr Lys
120         345                 350                 355
122 gaa gtg gag aga gga aag agt aaa tgt gtc aaa tac tgg cct gat gag    1275
123 Glu Val Glu Arg Gly Lys Ser Lys Cys Val Lys Tyr Trp Pro Asp Glu
124     360                 365                 370
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Input Set : A:\PTO.AMC.txt
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126 tat gct cta aaa gaa tat ggc gtc atg cgt gtt agg aac gtc aaa gaa    1323
127 Tyr Ala Leu Lys Glu Tyr Gly Val Met Arg Val Arg Asn Val Lys Glu
128 375                 380                 385                 390
130 agc gcc gct cat gac tat acg cta aga gaa ctt aaa ctt tca aag gtt    1371
131 Ser Ala Ala His Asp Tyr Thr Leu Arg Glu Leu Lys Leu Ser Lys Val
132                 395                 400                 405
134 gga caa ggg aat acg gag aga acg gtc tgg caa tac cac ttt cgg acc    1419
135 Gly Gln Gly Asn Thr Glu Arg Thr Val Trp Gln Tyr His Phe Arg Thr
136             410                 415                 420
138 tgg ccg gac cac ggc gtg ccc agc gac cct ggg ggc gtg ctg gac ttc    1467
139 Trp Pro Asp His Gly Val Pro Ser Asp Pro Gly Gly Val Leu Asp Phe
140         425                 430                 435
142 ctg gag gag gtg cac cat aag cag gag agc atc atg gat gca ggg ccg    1515
143 Leu Glu Glu Val His His Lys Gln Glu Ser Ile Met Asp Ala Gly Pro
144     440                 445                 450
146 gtc gtg gtg cac tgc agt gct gga att ggc cgg aca ggg acg ttc att    1563
147 Val Val Val His Cys Ser Ala Gly Ile Gly Arg Thr Gly Thr Phe Ile
148 455                 460                 465                 470
150 gtg att gat att ctt att gac atc atc aga gag aaa ggt gtt gac tgc    1611
151 Val Ile Asp Ile Leu Ile Asp Ile Ile Arg Glu Lys Gly Val Asp Cys
152                 475                 480                 485
154 gat att gac gtt ccc aaa acc atc cag atg gtg cgg tct cag agg tca    1659
155 Asp Ile Asp Val Pro Lys Thr Ile Gln Met Val Arg Ser Gln Arg Ser
156             490                 495                 500
158 ggg atg gtc cag aca gaa gca cag tac cga ttt atc tat atg gcg gtc    1707
159 Gly Met Val Gln Thr Glu Ala Gln Tyr Arg Phe Ile Tyr Met Ala Val
160         505                 510                 515
162 cag cat tat att gaa aca cta cag cgc agg att gaa gaa gag cag aaa    1755
163 Gln His Tyr Ile Glu Thr Leu Gln Arg Arg Ile Glu Glu Glu Gln Lys
164     520                 525                 530
166 agc aag agg aaa ggg cac gaa tat aca aat att aag tat tct cta gcg    1803
167 Ser Lys Arg Lys Gly His Glu Tyr Thr Asn Ile Lys Tyr Ser Leu Ala
168 535                 540                 545                 550
170 gac cag acg agt gga gat cag agc cct ctc ccg cct tgt act cca acg    1851
171 Asp Gln Thr Ser Gly Asp Gln Ser Pro Leu Pro Pro Cys Thr Pro Thr
172                 555                 560                 565
174 cca ccc tgt gca gaa atg aga gaa gac agt gct aga gtc tat gaa aac    1899
175 Pro Pro Cys Ala Glu Met Arg Glu Asp Ser Ala Arg Val Tyr Glu Asn
176             570                 575                 580
178 gtg ggc ctg atg caa cag cag aaa agt ttc aga tga gaaaacctgc        1945
179 Val Gly Leu Met Gln Gln Gln Lys Ser Phe Arg
180         585                 590
182 caaaacttca gcacagaaat agatgtggac tttcaccctc tccctaaaaa gatcaagaac  2005
184 agacgcaaga aagtttatgt gaagacagaa tttggatttg gaaggcttgc aatgtggttg  2065
186 actacctttt gataagcaaa atttgaaacc atttaaagac cactgtattt taactc      2121
189 <210> SEQ ID NO: 2
190 <211> LENGTH: 25
191 <212> TYPE: DNA
192 <213> ORGANISM: Artificial Sequence
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RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/031,044

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Input Set : A:\PTO.AMC.txt
Output Set: N:\CRF3\02142002\J031044.raw

194 <220> FEATURE:
195 <223> OTHER INFORMATION: PCR Primer
197 <400> SEQUENCE: 2
198 ctggagactt cacactttcc gttag
201 <210> SEQ ID NO: 3 25
202 <211> LENGTH: 24
203 <212> TYPE: DNA
204 <213> ORGANISM: Artificial Sequence
206 <220> FEATURE:
207 <223> OTHER INFORMATION: PCR Primer
209 <400> SEQUENCE: 3
210 gcccgtgatg ttccatgtaa tact
213 <210> SEQ ID NO: 4 24
214 <211> LENGTH: 31
215 <212> TYPE: DNA
216 <213> ORGANISM: Artificial Sequence
218 <220> FEATURE:
219 <223> OTHER INFORMATION: PCR Probe
221 <400> SEQUENCE: 4
222 ctgtcaccca catcaagatt cagaacactg g
225 <210> SEQ ID NO: 5 31
226 <211> LENGTH: 19
227 <212> TYPE: DNA
228 <213> ORGANISM: Artificial Sequence
230 <220> FEATURE:
231 <223> OTHER INFORMATION: PCR Primer
233 <400> SEQUENCE: 5
234 gaaggtgaag gtcggagtc
237 <210> SEQ ID NO: 6 19
238 <211> LENGTH: 20
239 <212> TYPE: DNA
240 <213> ORGANISM: Artificial Sequence
242 <220> FEATURE:
243 <223> OTHER INFORMATION: PCR Primer
245 <400> SEQUENCE: 6
246 gaagatggtg atgggatttc
249 <210> SEQ ID NO: 7 20
250 <211> LENGTH: 20
251 <212> TYPE: DNA
252 <213> ORGANISM: Artificial Sequence
254 <220> FEATURE:
255 <223> OTHER INFORMATION: PCR Probe
257 <400> SEQUENCE: 7
258 caagcttccc gttctcagcc
261 <210> SEQ ID NO: 8 20
262 <211> LENGTH: 20
263 <212> TYPE: DNA
264 <213> ORGANISM: Artificial Sequence
266 <220> FEATURE:

RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/031,044

DATE: 02/14/2002
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Input Set : A:\PTO.AMC.txt
Output Set: N:\CRF3\02142002\J031044.raw

267 <223> OTHER INFORMATION: Antisense Oligonucleotide
269 <400> SEQUENCE: 8
270 ggcccgctcg ggaccggacg
273 <210> SEQ ID NO: 9 20
274 <211> LENGTH: 20
275 <212> TYPE: DNA
276 <213> ORGANISM: Artificial Sequence
278 <220> FEATURE:
279 <223> OTHER INFORMATION: Antisense Oligonucleotide
281 <400> SEQUENCE: 9
282 tccgcgatgt catgttcctc
285 <210> SEQ ID NO: 10 20
286 <211> LENGTH: 20
287 <212> TYPE: DNA
288 <213> ORGANISM: Artificial Sequence
290 <220> FEATURE:
291 <223> OTHER INFORMATION: Antisense Oligonucleotide
293 <400> SEQUENCE: 10
294 aaaccatctc cgcgatgtca
297 <210> SEQ ID NO: 11 20
298 <211> LENGTH: 20
299 <212> TYPE: DNA
300 <213> ORGANISM: Artificial Sequence
302 <220> FEATURE:
303 <223> OTHER INFORMATION: Antisense Oligonucleotide
305 <400> SEQUENCE: 11
306 acggacccgc tccttgctca
309 <210> SEQ ID NO: 12 20
310 <211> LENGTH: 20
311 <212> TYPE: DNA
312 <213> ORGANISM: Artificial Sequence
314 <220> FEATURE:
315 <223> OTHER INFORMATION: Antisense Oligonucleotide
317 <400> SEQUENCE: 12
318 tgttcctccc gccctccggc
321 <210> SEQ ID NO: 13 20
322 <211> LENGTH: 20
323 <212> TYPE: DNA
324 <213> ORGANISM: Artificial Sequence
326 <220> FEATURE:
327 <223> OTHER INFORMATION: Antisense Oligonucleotide
329 <400> SEQUENCE: 13
330 catgttcctc ccgccctccg
333 <210> SEQ ID NO: 14 20
334 <211> LENGTH: 20
335 <212> TYPE: DNA
336 <213> ORGANISM: Artificial Sequence
338 <220> FEATURE:
339 <223> OTHER INFORMATION: Antisense Oligonucleotide

VERIFICATION SUMMARY
PATENT APPLICATION: US/10/031,044

DATE: 02/14/2002
TIME: 09:03:30

Input Set : A:\PTO.AMC.txt
Output Set: N:\CRF3\02142002\J031044.raw

L:11 M:270 C: Current Application Number differs, Replaced Current Application No
L:11 M:271 C: Current Filing Date differs, Replaced Current Filing Date